UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/225,502	01/06/1999	PAUL A. MOORE	PF392	2400

22195 7590 01/30/2002

HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

EXAMINER	
DECLOUX, AMY M	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/225,502	Moore, P. et al
Examiner	**Art Unit**
DeCloux, Amy	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Nov 20, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 21-56 and 58-103 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 21-56 and 58-103 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. The request filed 11-20-01 (Paper No. 26) for a continued Prosecution Application (CPA) under 37 CFR 1.53.(d) based on parent application No. 09/225,502, filed 1-16-99, is acceptable and a CPA has been established. An action on the CPA follows.

2. *35 U.S.C. § 101* reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, In such full, clear, concise, and exact terms as to enable any person skilled In the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 21-56 and 58-103 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, substantial, specific, or well-established utility.

Claims 21-56 and 58-103 are drawn to polynucleotides encoding proteins that have homology to the FK506 binding protein FKBP65 and methods of expressing these proteins, the proteins of SEQ ID NO: 6 and 8, nucleotides and proteins having 95% homology to SEQ ID NO:s 5-8, heterologous nucleic acid and polypeptides, complement, secreted vector, host cell, method of producing the polypeptides and pharmaceutical compositions thereof. The claimed polynucleotides and polypeptides are not supported by either a specific and substantial asserted utility or a well-established utility. The specification fails to provide objective evidence of any activity for the encoded proteins or to show that these proteins even exist. Applicant only states that the sequence has homology to the FK506 binding protein FKBP65. Therefore, SEQ ID Nos:5-8 have no well-established utility. A well-established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Identifying a polynucleotide as encoding a FKBP65-like protein does not endow the polynucleotide with such a utility. The instant specification discloses that FKBP65 is a FK506 binding protein and confers immunomodulating activity to FK506, rapamycin and cyclosporin A, (Page 6, lines 20-26 of the instant specification). Identifying a protein as having homology to FKBP65, does not indicate what function it and thus the encoding polynucleotide might have. There is no specific disease or specific function that is

suggested by this homology; no conserved regions that would indicate that the claimed polypeptides function similarly to FKBP65 are identified. There is therefore no specific, substantial, or credible utility that is well-known, apparent, or implied by the relationship of the instant polynucleotide to the polynucleotide encoding a FKBP65-like protein or fragments thereof, nor the FKBP65-like protein or fragments thereof, nor the claimed heterologous versions of said proteins and nucleic acids, nor the claimed complement of said nucleic acids, nor the claimed pharmaceutical compositions thereof, nor the claimed homologs of said proteins and nucleic acids, nor the claimed methods of producing the claimed polypeptides.

The claimed polynucleotides also lack a specific or substantial utility. The utilities identified by the applicant on beginning on page 22 are also not specific or substantial. A utility such as chromosome localization would apply to virtually every naturally occurring polynucleotide and is therefore not specific. Likewise, tissue-specific expression does not rely on specific properties or functions of the encoded protein, nor do uses including gene therapy, forensic uses and uses in molecular techniques such as Northern and Southern blots and antibody production. Further, the specification does not disclose any diseases or conditions known to be associated with the encoded protein, clearly further research would be required to identify a disease in which the encoded protein is involved and would be of significance; Therefore, the polynucleotide and the encoded polypeptide and derivatives thereof therefore lack a substantial utility. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. See also the Revised Interim Utility Guidelines available at www.uspto.gov.

5. Claims 21-56 and 58-103 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

6. Applicant traverses the 101 rejection and disagrees with the examiner's contention that the asserted utility of the claimed polynucleotides and corresponding polypeptides is neither specific nor substantial based merely on homology to FKBP65, and asserts that Wilson teaches that at least 40% identity corresponds to a sharing of a precise function, while sequence identities of about 25% comprise a functional class. However, the examiner contends that Wilson's definition of "functional class" and "precise function" is rather broad especially when the function of non-enzymatic proteins are compared, as evidenced by the second paragraph on page 243, which says that the non-enzyme classes are broader for precise function. For example, on page 244, Figure 6c shows that a protein involved in starch metabolism has the same precise function as a protein in glycogen metabolism, and page 242, column 2, the

second to the last paragraph says that arc repressor and c-jun have the same precise function because both are transcription factors. However, as one of skill in the art would not know how to use any transcription factor without knowing its specificity, similarly one of skill in the art would not know how to use the claimed nucleotides which encode polypeptides that have only a limited probability of functioning in a relatively broad classification. Given Wilson's broad functional classes and given a BLAST search shows that the overall homology of the recited amino acid sequences of SEQ ID NO:6 and SEQ ID NO:8 is less than 50% identical with FKBP65 which binds a potent immunosuppressant FK506, the examiner disagrees with applicant's contention that said low sequence homology provides sufficient specific and substantial utility for the proteins encoded by said SEQ ID NO:s being used for the treatment of diseases caused by overactive immune systems, especially in view of the lack of any functional guidance in the instant specification(other than sequence homology). Therefore though applicant's arguments have been carefully considered they are not deemed persuasive and the rejection is maintained, essentially for the reasons of record.

7. Claims 38-51 and 68-80 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has described the polynucleotide sequences consisting of SEQ ID NOs:5 and 7, as well as nucleotides encoding the amino acid sequence of SEQ ID NOs:6 and 8. However, the claims as written encompass polynucleotides that encode proteins with 95% homology to SEQ ID NO:s 6 and 8, that vary substantially in length and also in nucleotide composition. The instant disclosure of two nucleic acids, that of SEQ ID Nos:5 and 7, does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The specification discloses the isolated cDNA sequence SEQ ID NOs:5 and 7 and the translated amino acid sequence of SEQ ID NOs: 6 and 8. The specification does not provide evidence that the proteins of SEQ ID Nos:6 and 8 actually exist. There is no description of the required structural and functional features of said proteins, or of the conserved regions that would be critical for these features. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides encompassed.

Therefore, applicant has not disclosed sufficient species such that one skilled in the art would conclude that applicant was in possession of the claimed genus of polynucleotides encoding polypeptides 95% identical to SEQ ID NOs: 6 or 8.

Therefore, the structure of these elements is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus of nucleic acids, including genes, encompassed by the claimed invention.

8. Applicant traverses the written description rejection on the basis that 95% identity to SEQ ID NO:6 and 8 will inherently share some structural similarities, however the examiner contends that the instant specification does not disclose the structure sufficient for whatever immunosuppressant activity is purported to be displayed by the proteins of SEQ ID NO:6 or 8. Applicant further argues that one of skill in the art could make mutations in the polynucleotides encoding SEQ ID NO:6 or 8 to achieve a protein with 95% homology to SEQ ID NO:6 or 8 that still retains the function of SEQ ID NO: 6 or 8, which may be true if in fact one knew the functional activity of SEQ ID NO:6 or 8 in the first place. Applicant suggests that the variants of SEQ ID NO:6 and 8 could be tested for by the PPIase activity as described by Galat et al, but the instant specification does not disclose that SEQ ID NO:6 or 8 itself displays said activity.

Therefore though applicant's arguments have been carefully considered they are not deemed persuasive and the rejection is maintained, essentially for the reasons of record.

9. Claims 38-51 and 68-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 38-51 and 68-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for nucleic acid molecule encoding SEQ ID NO:6, and SEQ ID NO:8, does not reasonably provide enablement for a nucleic acid molecule comprising a nucleotide sequence encoding an amino acid sequence at least 95% identical with residues of SEQ ID NO:6 and SEQ ID NO:8, nor with nucleic acid molecules comprising heterologous sequences, recombinant vector, recombinant host cell, a method of producing said polypeptide, or a composition of said nucleic acid molecule.

Additionally, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required are summarized In *In re Wands* (858iF2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides the polynucleotides encoding polypeptides with the sequences SEQ ID NO:6, and SEQ ID NO:8, respectively, the specification fails to provide guidance as to how to make or use the claimed polynucleotide encoding a polynucleotide with at least an 95% identity to the claimed sequences. Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which nucleic acids in the nucleotide sequence, if any are tolerant of modification and which are conserved (ie., expectedly intolerant to modification), and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. However, the problem of predicting functional aspects of the product from mere sequence data of a single nucleic acid sequence and what changes can be tolerated is complex and well outside the realm of routine experimentation. *In re Fisher*, 1666 USPQ 19 24 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Without such guidance, the fragments which can be made and used to encode peptides of the claimed activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly extensive and undue. See *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

Therefore, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acid encoding the amino acid sequences broadly encompassed by the claims due to the significant number of untaught sequences. Therefore, there is no evidence of record to show that one skilled In the art would be able to practice the invention as claimed without an undue amount of experimentation.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance In the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. Applicant traverses the enablement rejection on the grounds that " since the disclosed or otherwise known methods of making and screening the claimed polypeptides may be used to determine without undue experimentation , whether a given polypeptide or variant thereof encompassed by the claims exhibits, for example, PPIase activity, the enablement requirement is fully satisfied." However, the examiner points out that the instant specification discloses insufficient guidance that the polypeptides of SEQ ID NO:6 or 8, or variants thereof, exhibit PPIase activity, or any

other activity for that matter. Therefore, though the skill in the molecular biology is high as stated by the applicant, the examiner contends that the function of the polypeptides of SEQ ID NO:6 or 8, or variants thereof, is unpredictable based on less than 50% homology with FKBP65 and it would require undue experimentation to practice the claimed invention in view of the insufficient guidance and direction in the instant specification on how to use said polypeptides, or variants thereof.

Therefore though applicant's arguments have been carefully considered they are not deemed persuasive and the rejection is maintained, essentially for the reasons of record.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Amy DeCloux, Ph.D.
Patent Examiner,
Group 1640, Technology Center 1600
January 29, 2002

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644